The advantages of CER: clinical, methodological, and political considerations

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Conflicts of interest

- Neither I nor any of my faculty accept any personal compensation of any kind from any drug or device manufacturer.
- Most of the research in my Division is funded by NIH / AHRQ / FDA.
- The Division occasionally accepts unrestricted research grants from industry to conduct specific drug-epi studies.
- All of my work on academic detailing is done through non-profit organizations, and I receive no payment for my participation.

Subtitle of the talk:

"Pharmaco-epistemology and the politics of knowledge"

What is “pharmaco-epistemology”?!

- definition: ***How we know what we know*** about drug benefits, risks, side effects, and cost-effectiveness.

- How can drug ***knowledge*** have ***politics***?
  - What we study and what we learn about medications is shaped by economic, cultural, and political factors as well as purely scientific ones.

What doctors, payers, patients, and policymakers need to know about a drug

- Its benefits, safety, and value (cost-effectiveness) ***in relation to other reasonable prescribing choices for a given condition.***
- How well the drug actually works in ***typical populations*** (effectiveness), not just in randomized controlled trials (efficacy).

By contrast: What the FDA approval process tells us

- How well a new product works when prescribed by **atypical doctors** treating a **small sample** of **volunteer patients** that **under-represents** several key populations in a **highly protocolized** trial design that is usually **brief**, may compare the new drug only to **placebo**, and may use a **surrogate measure** rather than actual clinical outcomes as its measure of efficacy.

A question that no patient ever asked me

"Dr. Avorn, could you please prescribe me a drug that's probably a little better than nothing?"

The current problem

- Until now, we have had no systematic way to know which treatments work best for common clinical problems.
  - Which are the most effective?
  - Which are the safest?
  - Which are the best value economically?

This hampers treatment decisions

- …for patients with:
  - diabetes
  - high blood pressure
  - atrial fibrillation
  - coronary artery disease
  - osteoporosis
  - stroke
  - cancer
  - etc., etc., etc., etc.

Generating the additional knowledge we need

- Previous poor adherence to FDA's "mandated post-market commitment" requirements
  - FDAAA may help remedy this
- Failure of the marketplace assumption
  - decades of experience that this doesn't produce the data we need
- Re-discovery of the concept of Public Goods
  - things that benefit all, funded by society
  - like highways, fire departments, clean air, police, education, defense

Examples of seminal CER studies

- ALLHAT
  - NHLBI-funded study of >30,000 patients with high blood pressure
  - found inexpensive thiazide-type drugs work as well as or better then more costly products
  - revolutionized how we treat hypertension
- Women's Health Initiative
  - NIH-funded study of estrogens and heart disease
  - demonstrated that some of the most widely used drugs in US were harmful

We are now entering a new era of expanded CER research

- initial $1.1 billion in ARRA
- great promise of PCORI
  - substantial, stable, ongoing funding
  - political vulnerability
  - *two-thousandths of a percent* of health care spend
    - *0.002%*
- can improve outcomes ***and*** help contain costs

Clinical and methodological issues

- Picking the right comparator(s)
  - may include drug vs. device vs. surgery
    - as well as “watchful waiting” for some conditions
- Studying ***typical*** care
  - in terms of patients, clinicians, settings
- Observational studies vs. randomized controlled trials
  - strengths, weaknesses of each
  - important methods issues in observational studies

    - See Avorn & Fischer, and Chokshi, Avorn, & Kesselheim, *Health Affairs, October 2010*

Lost in translation?
Two more missing ingredients

- Effective ***communication*** of CER findings to practitioners and policymakers
  - it won't disseminate itself

- ***Motivation*** *f*or clinicians and systems to take up these findings and use them to transform practice
  - to replace current incentives that are absent or perverse

Once comparative effectiveness studies are completed…

…we still have to transform these findings into improved patient care decisions.

Implementation issues

- Must avoid CER-based policies that are ham-handed, clinically obtuse, or unethical:
  - motivation based on stinginess or profit rather than appropriate care
  - excessively rigid formularies
  - lack of respect for real individual differences
  - contempt for physician's clinical acumen
  - draconian "prior authorization" requirements

“Academic detailing”: one way to get CER into practice

- scientific knowledge doesn’t disseminate itself
- interactive, clinically relevant ***educational outreach***, based on social marketing and pharma approach, can improve practice
  - without the product-sales agenda
- growth of programs
  - several U.S. states, HMOs
  - Federal: AHRQ, VA
    - See JAMA, Sept. 21, 2011
  - Europe, Australia, Canada

An academic detailing example

- The "Independent Drug Information Service" (iDiS):
  - impartial, evidence-based review of CER literature
  - production of user-friendly educational materials for MDs, patients
  - Educational outreach to MDs by specially trained RNs, pharmacists, MDs
  - runs academic detailing programs in several states
  - trains educators for other programs

Education can take us pretty far… but not all the way

- Most physicians would rather prescribe wisely than poorly.

  …it's just that most of us don't have access to the information we need.

- Better communication alone can't combat the perverse incentives of fee-for-service medicine
  - *"It is difficult to get a man to understand something when his salary depends on his not understanding it."* -- Upton Sinclair

Politics vs. science in CER

The “death panel” disinformation strategy

- No real basis for this in any law or regulation
- Generating new knowledge never denied needed care to anyone.
- Most denial of services results from lack of access…
  - …which is largely caused by the unaffordability of care
  - …which is largely the result of inefficient use of available resources.

-- Avorn, NEJM 2009

Individual differences in treatment response

The politics of "personalized medicine"

- Arguments about individual differences are used to undermine the validity of CER
  - pharmacogenetics
  - racial, gender, age disparities in drug effects
- Scare-terms to watch out for:
  - "Cookie-cutter/cookbook medicine"
  - "One size fits all"
  - "My patients are different"

Separating science from rhetoric

- Yes, there are some important examples of genetic variation influencing drug response.
  - e.g., Herceptin, some other oncology drugs
  - less responsiveness of blacks to ACE inhibitors
  - etc.
- We need to look for and study more such examples.
- These differences can be accommodated in rational, science-driven policies.
- But this is ***not*** a major issue in the vast majority of clinical prescribing decisions.
- CER can ***clarify***, rather than ignore these issues.

We need to elevate, not degrade the quality of our discourse

"Characteristics of Clinical Trials to Support Approval of Orphan vs Non-orphan Drugs for Cancer."

Kesselheim AS, Myers JA, Avorn J. JAMA 2011

Findings: Orphan drugs for cancer were far more likely to:

- be approved on the basis of inadequate trial designs
  - often lacking control groups or blinding
- not assess patient survival
- cause serious adverse effects

Concern: patients given orphan drugs may be less likely to benefit than patients given drugs that are more adequately studied.

Recommendation: improve the quality of orphan drug trials.

“Jerry Avorn has been a long time malignant presence on the health policy scene...Avorn, Kesselheim and Myers to kids dying of rare disease: Drop dead while we study you as long as we deem it appropriate....

CER, by design…deliberately delays progress by demanding studies that, by ignoring individual differences, conclude no one benefits from medical progress. It is used to justify rationing, not make individuals more sustainable.

To save ourselves and children dying of rare diseases we have to pull the plug on CER and it’s adherents. Starting with Kessleheim, Myers and Avorn -- Harvard's Kevorkian Krew -- is a great place to start.”

Dr. Robert Goldberg, Co-founder and VP, Center for Medicine in the Public Interest, June 16, 2011 on www. Drugwonks.com

Demagoguery and hate-speech should have no place in civilized debates about science or health policy.

We must not let discussions of CER or other approaches to improve medical care sink to the same low level as other aspects of our national political discourse.

Conclusion

- Much of the care Americans receive is suboptimal and/or very overpriced.
- Methodologically rigorous CER can help us move toward improved quality and affordability for all patients.
- To do this, it will have to be effectively deployed throughout a health care system that is re-engineered to make proper use of this vitally important new knowledge.

For more information….

"Powerful Medicines: the Benefits, Risks, and Costs of Prescription Drugs"

(Knopf, 2005):

www.PowerfulMedicines.org

The BWH Division of Pharmaco-epi and Pharmaco-eco ("DoPE"):

www. DrugEpi.org

Academic detailing:

www. RxFacts.org

www. NaRCAD.org